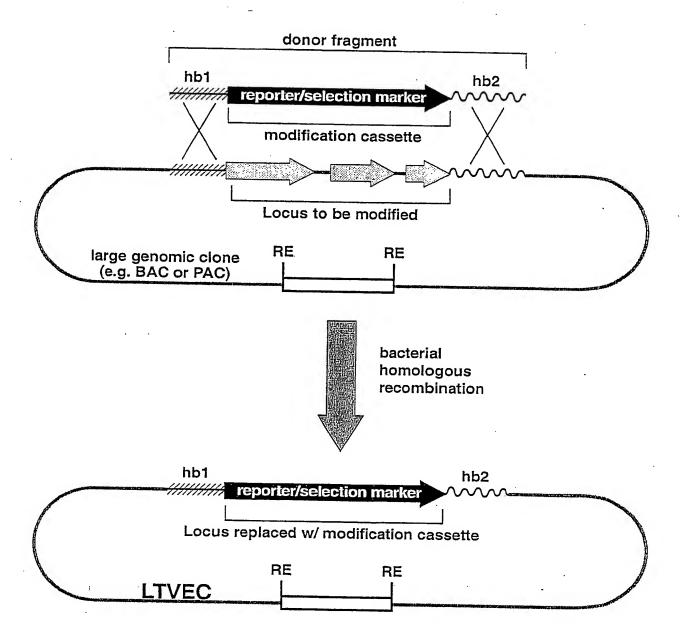
Figure 1



) 2

Figure 2

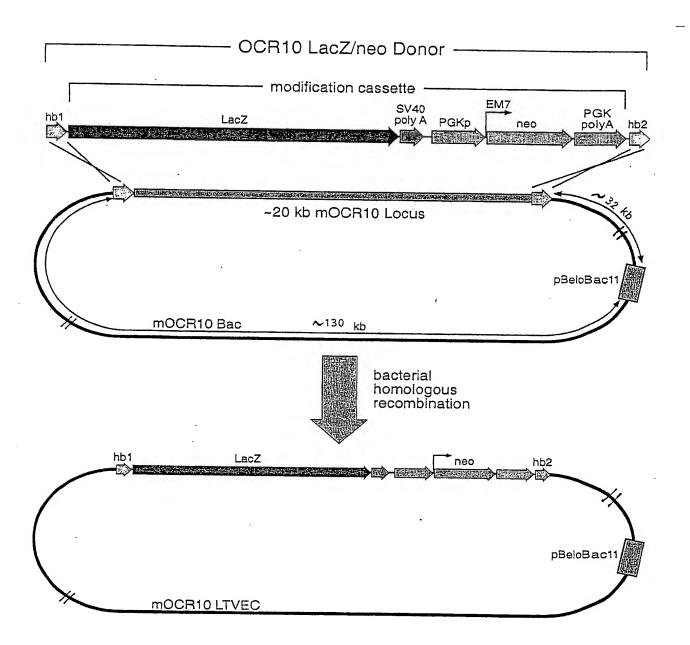


FIGURE 3A

		10		2	20		30)		40			50		60
CCC	CGGG	TT	CCTGI			AAGA		-	TAGO			ልጥርር		אהרר	TCATCT
GGG	GCCC	AA:	GGAC	AGAT	ילר שו	ىش كىشر	יאייהי	ACC	ZATO:	מב מביב מב מביב	GGG	771 GG	CCA		AGTAGA
									J. 1 1 C \	22100	366	incc	CGA	1166	AG I AGA
		70		5	30		90)		100			110		120
TTG	GTACT	CA.	ACAGO	GGTC	T T	TTT			reggi					ጥርጥር	GCAGGG
AAC	CATG	AGT	TGTCC	CCAG	A A	GAAA	ראכיתכ	CA	שמררי מנוררי	TCCT	CCA	מממם	YCT.		CGTCCC
											0011	QLLLL	1101	nchc	001000
	-	130		14	ł 0		150)		160			170		180
ACT	GACC	CTG	GGTGC	GGA	G C	CACTO	CAGTO	CA'	TGAC					רברב	TATACC
TGA	CTGG	GAC	CCAC	CCTI	C G	GTGA	STCAC	GT	ACTG	GGT	CGA	CCAA	GTG	CTCT CTCT	ATATGG
											00.1		010	0101.	AIAIGG
	:	190		20	00		210)			220			23	0
ACA'	TACT	PTT	CTTG	AGG	C T	GGA(CACAC	3 C 2	ATG (caa .	CGG	GGC ·	CCA		GCT GCC
TGT.	ATGA	AAA	GAAC	TCC	AG A	CCCT	STGTO	G '	TAC (GGG (GCC	CCG -	GGT	CAC	CGA CGG
															Ala Ala>
;	240			250			26	50			270			280	
ATT	CTC	CTG	CTG	ATT	CTC	CAT	GGA	GCT	TGG	AGC	TGC	CTG	GAC	CTC	ACT
AAT	GAG	GAC	GAC	TAA	GAG	GTA	CCT	CGA	ACC	TCG	ACG	GAC	CTG	GAG	TGA
Leu	Leu	Leu	Leu	Ile	Leu	His	Gly	Ala	Trp	Ser	Cys	Leu	Asp	Leu	Thr>
											_		_		
		90			300			310				20			330
			GAC												
ACG	ATG	TGA	CTG	ATG	,GAG	ACC	TGG	TAG	TGG	ACA	CAG	GAC	CTC	TGT	GCC
Cys	Tyr	Thr	Asp	Tyr	Leu	Trp	Thr	Ile	Thr	Cys	Val	Leu	Glu	Thr	Arg>
		340				50			360			370			
AGC	CCC	AAC	CCC	AGC	ATA	CTC	AGT	CTC	ACC	TGG	CAA	GAT	GAA	TAT	GAG
TCG	GGG	TTG	GGG	TCG	TAT	GAG	TCA	GAG	TGG	ACC	GTT	CTA	CTT	ATA	CTC
ser	bro	Asn	Pro	Ser	Ile	Leu	Ser	Leu	Thr	Trp	Gln	Asp	Glu	Tyr	Glu>
380			300			400									
	Cmm		390	C1 70 70	C 2 C	400	mma	maa		10	~		420		
CUU	CII	CMG	GAC	CAA	GAG	ACC	TTC	TGC	AGC	CTA	CAC	AAG	TCT	GGC	CAC
CII	TON	G10	CTG	GIT	CTC	17GG	AAG.	ACG	TCG	GAT	GTG	TTC	AGA	CCG	GTG
GIU	neu	GTII	. Asp	GTH	GIU	1111	Pne	Cys	ser	ьеп	HIS	гЛЗ	Ser	GIY	His>
430			4	10		,	150			460			A	7.0	
		מים	. CAT		TCC			TCC	C M		000	mma		70	mmo.
			GTA												
															Phe>
						- 2 -	1111	Cys	1115	IIE C	Arg	Deu	ser	GIII	Phe>
	480			490			5.0	00		1	510	,		520	
		GAT	GAA		TTC	ATT			GTG			CÁG	ىلى ك		AAC
GAC	AGG	CTA	CTT	CAA	AAG	TAA	CAG	TTG	CAC	TGC	СТС	GTC	ACA	ככפ	TTG
Leu	Ser	Asp	Glu	Val	Phe	Ile	Val	Asn	Val	Thr	Asp	Gln	Ser	Glv	Asn>
		_											~		
	5	30		Ţ	540			550			5	60			570
AAC	TCC	CAA	GAG	TGT	GGC	AGC	TTT	GTC	CTG	GCT			ATC		
TTG	AGG	GTI	CTC	ACA	CCG	TCG	AAA	CAG	GAC	CGA	CTC	TCG	TAG	TTC	GGT
Asn	Ser	Gln	Glu	Cys	Gly	Ser	Phe	Val	Leu	Ala	Glu	Ser	Ile	Lys	Pro>

,

FIGURE 3B

			580			,										
	CCT			mmc	220		90	~~~		500			610			
	CCA	CCC	CCC	1"I'G	AAC	GIG	ACT	GTG	GCC	TTC	TCA	GGA	CGC	TAT	GAT	ATC
	NI ~	D	D	AAC	7.1.G	CAC	TGA	CAC	CGG	AAG	AGT	CCT	GCG	ATA	CTA	TAG
	Ald	Pro	Pro	ьeu	Asn	Val	'l'nr	Val	Ala	Phe	Ser	Gly	Arg	Tyr	Asp	Ile>
62	0		630 GAC TCA GCT TAT				640			650			660			
	TCC	TGG	GAC	TCA	$GC\overline{T}$	TAT	GAC	GAA	ccc			TAC			AGA	GGC
	AGG	ACC	CTG	AGT	CGA	ATA	CTG	CTT	GGG	AGG	TTG	ATG	CAC	CAC	TOT	CCG
	Ser	Trp	Asp	Ser	Ala	Tyr	Asp	Glu	Pro	Ser	Asn	Tvr	Val	Leu	Ara	Gly>
•															5	01 ,
	670	~~~			30			590			700				10	
	AAG	CTA	CAA	TAT	GAG	CTG	CAG	TAT	CGG	AAC	CTC	AGA	GAC	CCC	TAT	GCT
	The	GAT.	GTT	ATA	CTC	GAC	GTC	ATA	GCC	TTG	GAG	TCT	CTG	GGG	ATA	CGA
	гÃг	டeu	GIN	Tyr	GIu	Leu	Gln	Tyr	Arg	Asn	Leu	Arg	Asp	Pro	Tyr	Ala>
		720			730			7.	10			7 - 0			T 6 0	
			CCG	CTC		א א כי	CTC	-		CMC		750			760	TCT
	C 2 C	ערר	CCC	CAC	TCC	ששט	CIG	MYC	1 CM	GIG	GAC	TCA	AGA	AAC	GTC	AGA
	Val	Ara	Pro	Val	Thr	TATE	TAU	TIAG	AG1	UAC	700	AGT	TCT	7.1.0	CAG	AGA Ser>
		9		VUL	1 111	шyз	пеа	116	Set	vaı	Asp	ser	Arg	ASI	Val	Ser>
			7 0			780			790				00		8	310
	CTT	CTC	CCT	GAA	GAG	TTC	CAC	AAA	GAT	TCT	AGC	TAC	CAG	CTG	CAG	ATG
	GAA	GAG	GGA	CTT	CTC	AAG	GTG	TTT	CTA	AGA	TCG	ATG	GTC	GAC	GTC	TAC
	Leu	Leu	Pro	Glu	Glu,	Phe	His	Lys	qzA	Ser	Ser	Tyr	Gln	Leu	Gln	Met>
			820			87	8 N	•	s	840			DEA			
	CGG	GCA	820 GCG	CCT	CAG		3 0 GGC	ACT		340 ~~~	A C C	ecc	850 ACC	TCC.	እ <i>ር</i> መ	CAC
	CGG GCC	GCA CGT	GCG	CCT GGA	CAG GTC	CCA	GGC	ACT	TCA	TTC	AGG	GGG	ACC	TGG	AGT	GAG
	GCC	CGT	GCG CGC	GGA	GTC	CCA GGT	GGC CCG	TGA	TCA AGT	TTC AAG	TCC	CCC	ACC TGG	ACC	TCA	CTC
	GCC	CGT	GCG CGC	GGA	GTC	CCA GGT	GGC CCG	TGA	TCA AGT	TTC AAG	TCC	CCC	ACC TGG	ACC	TCA	GAG CTC Glu>
86	GCC Arg 0	CGT Ala	GCG CGC Ala	GGA Pro 370	GTC Gln	CCA GGT Pro	GGC CCG Gly 880	TGA Thr	TCA AGT Ser	TTC AAG Phe	TCC Arg	Gly	ACC TGG Thr	ACC Trp	TCA Ser	CTC Glu>
86	GCC Arg 0 TGG	CGT Ala AGT	GCG CGC Ala GAC	GGA Pro 370 CCC	GTC Gln GTC	CCA GGT Pro	GGC CCG Gly 880 TTT	TGA Thr CAG	TCA AGT Ser	TTC AAG Phe 89 CAG	TCC Arg 0 GCT	GGG Gly	ACC TGG Thr	ACC Trp 900 CCC	TCA Ser GAG	CTC Glu>
86	GCC Arg 0 TGG ACC	CGT Ala AGT TCA	GCG CGC Ala GAC CTG	GGA Pro 370 CCC GGG	GTC Gln GTC CAG	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA	TGA Thr CAG GTC	TCA AGT Ser ACC TGG	TTC AAG Phe 89 CAG GTC	TCC Arg 0 GCT CGA	GGG CCC	ACC TGG Thr GAG CTC	ACC Trp 000 CCC GGG	TCA Ser GAG CTC	CTC Glu> GCA CGT
86	GCC Arg 0 TGG ACC	CGT Ala AGT TCA	GCG CGC Ala GAC CTG	GGA Pro 370 CCC GGG	GTC Gln GTC CAG	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA	TGA Thr CAG GTC	TCA AGT Ser ACC TGG	TTC AAG Phe 89 CAG GTC	TCC Arg 0 GCT CGA	GGG CCC	ACC TGG Thr GAG CTC	ACC Trp 000 CCC GGG	TCA Ser GAG CTC	CTC Glu>
86	GCC Arg 0 TGG ACC Trp	CGT Ala AGT TCA	GCG CGC Ala GAC CTG	GGA Pro 370 CCC GGG Pro	GTC Gln GTC CAG Val	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln	TCA AGT Ser ACC TGG	TTC AAG Phe 89 CAG GTC	TCC Arg 0 GCT CGA Ala	GGG CCC	ACC TGG Thr GAG CTC	ACC Trp 900 CCC GGG Pro	TCA Ser GAG CTC Glu	CTC Glu> GCA CGT
86	GCC Arg 0 TGG ACC Trp 910	AGT TCA Ser	GCG CGC Ala GAC CTG Asp	GGA Pro 370 CCC GGG Pro	GTC Gln GTC CAG Val	CCA GGT Pro ATC TAG	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln	TCA AGT Ser ACC TGG Thr	TTC AAG Phe 89 CAG GTC Gln	TCC Arg 0 GCT CGA Ala	GGG GGG GCG GCG GCC	ACC TGG Thr GAG CTC Glu	ACC Trp 000 CCC GGG Pro	TCA Ser GAG CTC Glu	CTC Glu> GCA CGT Ala>
86	GCC Arg 0 TGG ACC Trp 910 GGC	CGT Ala AGT TCA Ser	GCG CGC Ala GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT	GTC Gln GTC CAG Val	CCA GGT Pro ATC TAG .Ile	GGC CCG Gly 880 TTT AAA Phe	TGA Thr CAG GTC Gln 30 CTG	TCA AGT Ser ACC TGG Thr	TTC AAG Phe 89 CAG GTC Gln	TCC Arg 0 GCT CGA Ala 940 GCT	GGG Gly GGG Gly	ACC TGG Thr GAG CTC Glu	ACC Trp 900 CCC GGG Pro	TCA Ser GAG CTC Glu	CTC Glu> GCA CGT Ala>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG	AGT TCA Ser TGG ACC	GCG CGC Ala GAC CTG Asp GAC CTG	GGA Pro 370 CCC GGG Pro 92 CCT GGA	GTC Gln GTC CAG Val 20 CAC GTG	CCA GGT Pro ATC TAG Ile	GGC CCG Gly 880 TTT AAA Phe CTG GAC	TGA Thr CAG GTC Gln 30 CTG GAC	TCA AGT Ser ACC TGG Thr	TTC AAG Phe 89 CAG GTC Gln CTG GAC	TCC Arg 0 GCT CGA Ala 940 GCT CGA	GGG GLY GTC CAG	ACC TGG Thr GAG CTC Glu TTG AAC	ACC Trp 900 CCC GGG Pro 95 ATC	TCA Ser GAG CTC Glu 50 ATT TAA	CTC Glu> GCA CGT Ala> GTC CAG
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG	AGT TCA Ser TGG ACC	GCG CGC Ala GAC CTG Asp GAC CTG	GGA Pro 370 CCC GGG Pro 92 CCT GGA	GTC Gln GTC CAG Val 20 CAC GTG	CCA GGT Pro ATC TAG Ile	GGC CCG Gly 880 TTT AAA Phe CTG GAC	TGA Thr CAG GTC Gln 30 CTG GAC	TCA AGT Ser ACC TGG Thr	TTC AAG Phe 89 CAG GTC Gln CTG GAC	TCC Arg 0 GCT CGA Ala 940 GCT CGA	GGG GLY GTC CAG	ACC TGG Thr GAG CTC Glu TTG AAC	ACC Trp 900 CCC GGG Pro 95 ATC	TCA Ser GAG CTC Glu 50 ATT TAA	CTC Glu> GCA CGT Ala>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro	GTC Gln GTC CAG Val 20 CAC GTG His	CCA GGT Pro ATC TAG Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln 30 CTG GAC Leu	TCA AGT Ser ACC TGG Thr CTC GAG Leu	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala	GGG GLY GTC CAG Val	ACC TGG Thr GAG CTC Glu TTG AAC Leu	ACC Trp 900 CCC GGG Pro 95 ATC TAG Ile	TCA Ser GAG CTC Glu 60 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro	GTC Gln GTC CAG Val 20 CAC GTG His	CCA GGT Pro ATC TAG Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln 30 CTG GAC Leu 98 ATC	TCA AGT Ser ACC TGG Thr CTC GAG Leu 30 CAC	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala	GGG CCC Gly GTC CAG Val	ACC TGG Thr GAG CTC Glu TTG AAC Leu	ACC Trp 900 CCC GGG Pro 95 ATC TAG Ile	GAG CTC Glu 60 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA	CCA GGT Pro ATC TAG Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln 30 CTG GAC Leu 98 ATC TAG	TCA AGT Ser ACC TGG Thr CTC GAG Leu CAC GTG	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu CTG GAC	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala	GGG GCC GLY GTC CAG Val TGG ACC	ACC TGG Thr GAG CTC Glu TTG AAC Leu	ACC Trp 900 CCC GGG Pro 95 ATC TAG Ile CTA GAT	GAG CTC Glu 60 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val> AAA TTT
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA	CCA GGT Pro ATC TAG Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln 30 CTG GAC Leu 98 ATC TAG	TCA AGT Ser ACC TGG Thr CTC GAG Leu CAC GTG	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu CTG GAC	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala	GGG GCC GLY GTC CAG Val TGG ACC	ACC TGG Thr GAG CTC Glu TTG AAC Leu	ACC Trp 900 CCC GGG Pro 95 ATC TAG Ile CTA GAT	GAG CTC Glu 60 ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG	AGT TCA Ser TGG ACC Trp	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG	GTC Gln GTC CAG Val CAC GTG His 970 GGT CCA Gly	CCA GGT Pro ATC TAG Ile ATG TAC Met	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu	TGA Thr CAG GTC Gln CTG GAC Leu 98 ATC TAG Ile	TCA AGT Ser ACC TGG Thr CTC GAG Leu CAC GTG	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu CTG GAC	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala	GGG GLY GTC CAG Val B90 TGG ACC Trp	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 900 CCC GGG Pro 95 ATC TAG Ile CTA GAT	GAG CTC Glu ATT TAA Ile	CTC Glu> GCA CGT Ala> GTC CAG Val> AAA TTT Lys>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG GAC Leu	AGT TCA Ser TGG ACC Trp CAA Val	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG TAC Met	GTC Gln GTC CAG Val CAC GTG His 970 GGT CCA Gly	CCA GGT Pro ATC TAG Ile ATG TAC Met CTG GAC Leu	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln CTG GAC Leu 98 ATC TAG Ile	ACC TGG Thr CTC GAG Leu CAC GTG His	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu CTG GAC Leu	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala CCT GGA Pro	GGG CCC Gly GTC CAG Val E90 TGG ACC Trp	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 000 CCC GGG Pro ATC TAG Ile CTA GAT Leu	GAG CTC Glu 50 ATT TAA Ile 1000 TGG ACC Trp	GCA CGT Ala> GTC CAG Val> AAA TTT Lys>
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG GAC Leu	AGT TCA Ser TGG ACC Trp CAA Val 10:	GCG CGC Ala GAC CTG Asp GAC CTG Asp	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG TAC Met	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly	CCA GGT Pro ATC TAG Ile ATG TAC Met CTG GAC Leu	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln CTG GAC Leu 98 ATC TAG Ile ACC	ACC TGG Thr CTC GAG Leu CAC GTG His	TTC AAG Phe 89 CAG GTC GIn CTG GAC Leu CTG GAC Leu	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala CCT GGA Pro	GGG CCC Gly GTC CAG Val 90 TGG ACC Trp 104	ACC TGG Thr SAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00 CCC GGG Pro ATC TAG Ile CTA GAT Leu	GAG CTC Glu 50 ATT TAA Ile 5000 TGG ACC TTP	GCA CGT Ala> GTC CAG Val> AAA TTT Lys> 050 CTG
86	GCC Arg 0 TGG ACC Trp 910 GGC CCG Gly CTG GAC Leu AAG	AGT TCA Ser TGG ACC Trp CAA Val 10: ATA TAT	GCG CGC Ala GAC CTG Asp GAC CTG Asp TTC AAG Phe	GGA Pro 370 CCC GGG Pro 92 CCT GGA Pro ATG TAC Met	GTC Gln GTC CAG Val 20 CAC GTG His 970 GGT CCA Gly 10 CCA GGT	CCA GGT Pro ATC TAG Ile ATG TAC Met CTG GAC Leu 20 GTG CAC	GGC CCG Gly 880 TTT AAA Phe CTG GAC Leu AAG TTC Lys	TGA Thr CAG GTC Gln 30 CTG GAC Leu ATC TAG Ile ACC TGG	ACC TGG Thr CTC GAG Leu CAC GTG His	TTC AAG Phe 89 CAG GTC Gln CTG GAC Leu CTG GAC Leu GAG CTC	TCC Arg 0 GCT CGA Ala 940 GCT CGA Ala CCT GGA Pro	GGG CCC Gly GTC CAG Val 90 TGG ACC Trp 104 TTC AAG	ACC TGG Thr GAG CTC Glu TTG AAC Leu AGG TCC Arg	ACC Trp 00 CCC GGG Pro ATC TAG Ile CTA GAT Leu CAG GTC	GAG CTC Glu O ATT TAA Ile OOO TGG ACC Trp CCC GGG	GCA CGT Ala> GTC CAG Val> AAA TTT Lys> 050 CTG

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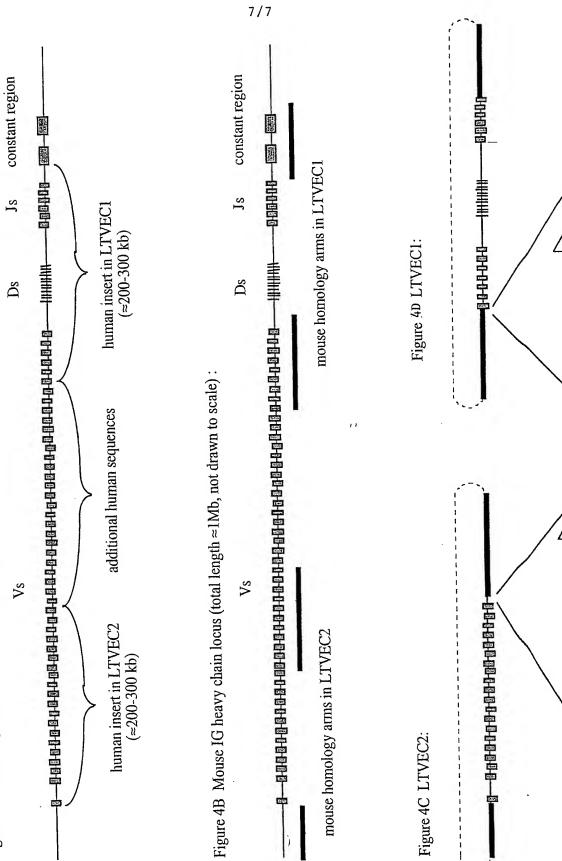
FIGURE 3C

	1	060			107	'n		1 (0.80			1090				
ТАС			CAC	A GC			ጥጥር			TOC			200	000	TTC	
ATG	TCC	CTC	GTG	TCG	CCC	ጥጥር	DAG	44C	ىلىنلىن چىچى	ACC.	CVV	עועה צי ביציד	TCC	CCI	AAG	
Tvr	Ara	Glu	His	Ser	Glv	Acn	Phe	TAVE	Tare	TCC.	UAA	1177	76G	Dwa	AAG Phe>	
-3-	9			201	CIY	11:511	1110	Lys	шys	1110	Val	ASII	1111	PIO	PHez	
1100		11	110		1	120			11:	30		1:	140			
ACG	GCC	TCC	AGC	ATA	GAG	TTG	GTG	CCA	CAG	AGT	TCC	ACA	ACA	ACA	TCA	
TGC	CGG	AGG	TCG	TAT	CTC	AAC	CAC	GGT	GTC	TCA	AGG	TGT	TGT	TGT	AGT	
Thr	Ala	Ser	Ser	Ile	Glu	Leu	Val	Pro	Gln	Ser	Ser	Thr	Thr	Thr	Ser>	
1150			116				170			1180			112			
GCC	ATT	CAT	CTG	TCA	TTG	TAT	CCA	GCC	AAG	GAG	AAG	AAG	TTC	CCG	GGG	
CGG	\mathbf{AAT}	GTA	GAC	AGT	AAC	ATA	GGT.	CGG	TTC	CTC	TTC	TTC	AAG	GGC	CCC	
Ala	Leu	His	Leu	Ser	Leu	Tyr	Pro	Ala	Lys	Glu	·Lys	Lys	Phe	Pro	Gly>	
1 1	200			1210			12:	2.0		٠,	220					
		CCT			CNC	ממת			mcm		230	3 m/a		1240	CCT	
GAC	CCC	CCA	CAC	GUU	CTC	CUM	CIG	CTC	161	GAT	COM	ATG	J.C.T.	GAG	GGA	
Tien	Pro	Gly	T.All	Glu	Glu	Cln	Lau	C10	Cara	Acn	CCT	Mat	AGA	010	Pro>	
·	110	GTA	neu	GIU	GIU	G711	neu	Glu	Cys	Asp	GIĀ	met	ser	GIU	PIO>	
	125	-			260		1270				128			1290		
GGT	CAC	TGG	TGC	ATA	ATC	CCC	TTG	GCA	GCT	GGC	CAA	GCG	GTC	TCA	GCC	
CCA	GTG	ACC	ACG	TAT	TAG	GGG	AAC	CGT	CGA	CCG	GTT	CGC	CAG	AGT	CGG	
Gly	His	Trp	Cys	Ile.	,Ile	Pro	Leu	Ala	Ala	Gly	Gln	Ala	Val	Ser	Ala>	
		1300			13.	0.0		1 -	320			1330				
TAC		L300 GAG	GAG	AGA	13: GAC		CCA		320 GGT	ሮሞር		1330	אוויידי	כאכ	አ ር አ	
TAC ATG	AGT	GAG	GAG CTC	AGA TCT	GAC	CGG	CCA	TAT	GGT	CTG	GTG	TCC	ATT	GAC	ACA	
ATG	AGT TCA	GAG CTC	CTC	TCT	GAC CTG	CGG GCC	GGT	TAT ATA	GGT CCA	GAC	GTG CAC	TCC AGG	TAA	CTG	TGT	
ATG	AGT TCA	GAG CTC	CTC	TCT	GAC CTG	CGG GCC	GGT	TAT ATA	GGT CCA	GAC	GTG CAC	TCC AGG	TAA	CTG	ACA TGT Thr>	
ATG	AGT TCA	GAG CTC Glu	CTC	TCT	GAC CTG Asp	CGG GCC	GGT	TAT ATA	GGT CCA	GAC Leu	GTG CAC	TCC AGG Ser	TAA	CTG	TGT	
ATG Tyr 1340 GTG	AGT TCA Ser	GAG CTC Glu 13 GTG	CTC Glu 350 GGA	TCT Arg GAT	GAC CTG Asp GCA	CGG GCC Arg L360 GAG	GGT Pro	TAT ATA Tyr	GGT CCA Gly 13	GAC Leu 70 GTC	GTG CAC Val	TCC AGG Ser 1: CCC	TAA Ile 380 TGT	CTG Asp AGC	TGT Thr>	
ATG Tyr 1340 GTG CAC	AGT TCA Ser ACT TGA	GAG CTC Glu 13 GTG CAC	CTC Glu 350 GGA CCT	TCT Arg GAT CTA	GAC CTG Asp GCA CGT	CGG GCC Arg 1360 GAG CTC	GGT Pro GGC CCG	TAT ATA Tyr CTG GAC	GGT CCA Gly 13 TGT ACA	GAC Leu 70 GTC CAG	GTG CAC Val TGG ACC	TCC AGG Ser 1: CCC GGG	TAA Ile 380 TGT ACA	CTG Asp AGC TCG	TGT Thr>	
ATG Tyr 1340 GTG CAC	AGT TCA Ser ACT TGA	GAG CTC Glu 13 GTG CAC	CTC Glu 350 GGA CCT	TCT Arg GAT CTA	GAC CTG Asp GCA CGT	CGG GCC Arg 1360 GAG CTC	GGT Pro GGC CCG	TAT ATA Tyr CTG GAC	GGT CCA Gly 13 TGT ACA	GAC Leu 70 GTC CAG	GTG CAC Val TGG ACC	TCC AGG Ser 1: CCC GGG	TAA Ile 380 TGT ACA	CTG Asp AGC TCG	TGT Thr>	
ATG Tyr 1340 GTG CAC Val	AGT TCA Ser ACT TGA	GAG CTC Glu 13 GTG CAC	CTC Glu 350 GGA CCT Gly	TCT Arg GAT CTA Asp	GAC CTG Asp GCA CGT	CGG GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly	TAT ATA Tyr CTG GAC	GGT CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val	GTG CAC Val TGG ACC	TCC AGG Ser 1: CCC GGG	TAA Ile 380 TGT ACA Cys	CTG Asp AGC TCG Ser	TGT Thr>	
ATG Tyr 1340 GTG CAC Val	AGT TCA Ser ACT TGA Thr	GAG CTC Glu 13 GTG CAC Val	CTC Glu 350 GGA CCT Gly	TCT Arg GAT CTA Asp	GAC CTG Asp GCA CGT Ala	CGG GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly	TAT ATA Tyr CTG GAC Leu	GGT CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val	GTG CAC Val TGG ACC Trp	TCC AGG Ser 1: CCC GGG Pro	TAA Ile 380 TGT ACA Cys	ASP AGC TCG Ser	TGT Thr> TGT ACA Cys>	
ATG Tyr 1340 GTG CAC Val 1390 GAG	AGT TCA Ser ACT TGA Thr	GAG CTC Glu 13 GTG CAC Val	GTC Glu 350 GGA CCT Gly 140 GGC	TCT Arg GAT CTA Asp	GAC CTG Asp GCA CGT Ala	CGG GCC Arg 1360 GAG CTC Glu	GGT Pro GGC CCG Gly 410 ATG	TAT ATA Tyr CTG GAC Leu	GGT CCA Gly 13 TGT ACA Cys	GAC Leu 70 GTC CAG Val 1420 GAT	GTG CAC Val TGG ACC Trp	TCC AGG Ser 1: CCC GGG Pro	TAA Ile 380 TGT ACA Cys 143 AGA	AGC TCG Ser	TGT TGT ACA Cys>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC	AGT TCA Ser ACT TGA Thr	GAG CTC Glu 13 GTG CAC Val	GTC Glu 350 GGA CCT Gly 140 GGC CCG	TCT Arg GAT CTA Asp 00 TAT ATA	GAC CTG Asp GCA CGT Ala CCA GGT	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG	GGT Pro GGC CCG Gly 410 ATG TAC	TAT ATA Tyr CTG GAC Leu AAC TTG	GGT CCA Gly 13 TGT ACA Cys CTG GAC	GAC Leu 70 GTC CAG Val 1420 GAT CTA	GTG CAC Val TGG ACC Trp GCT CGA	TCC AGG Ser 1: CCC GGG Pro	TAA Ile 380 TGT ACA Cys 143 AGA TCT	AGC TCG Ser 30 GAG CTC	TGT TGT ACA Cys>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC	AGT TCA Ser ACT TGA Thr	GAG CTC Glu 13 GTG CAC Val	GTC Glu 350 GGA CCT Gly 140 GGC CCG	TCT Arg GAT CTA Asp 00 TAT ATA	GAC CTG Asp GCA CGT Ala CCA GGT	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG	GGT Pro GGC CCG Gly 410 ATG TAC	TAT ATA Tyr CTG GAC Leu AAC TTG	GGT CCA Gly 13 TGT ACA Cys CTG GAC	GAC Leu 70 GTC CAG Val 1420 GAT CTA	GTG CAC Val TGG ACC Trp GCT CGA	TCC AGG Ser 1: CCC GGG Pro	TAA Ile 380 TGT ACA Cys 143 AGA TCT	AGC TCG Ser 30 GAG CTC	TGT TGT ACA Cys>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu	AGT TCA Ser ACT TGA Thr GAT CTA Asp	GAG CTC Glu 13 GTG CAC Val GAT CTA Asp	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly	TCT Arg GAT CTA Asp O TAT ATA Tyr	GAC CTG Asp GCA CGT Ala CCA GGT Pro	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	TAT ATA Tyr CTG GAC Leu AAC TTG ASn	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp	GTG CAC Val TGG ACC Trp GCT CGA Ala	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg	AGC TCG Ser 30 GAG CTC Glu	TGT TGT ACA Cys> TCT AGA Ser>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1. GGT	AGT TCA Ser ACT TGA Thr GAT CTA Asp	GAG CTC Glu 13 GTG CAC Val GAT CTA Asp	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly	TCT Arg GAT CTA Asp 00 TAT ATA Tyr	GAC CTG Asp GCA CGT Ala CCA GGT Pro	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala	GGT Pro GGC CCG Gly 410 ATG TAC Met	TAT ATA TYr CTG GAC Leu AAC TTG ASn 50 TTG	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA Asp	TGG ACC Trp GCT CGA Ala	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly CCT	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg	AGC TCG Ser GAG CTC Glu	TGT ACA Cys> TCT AGA Ser>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1390 GCTC CCA	AGT TCA Ser ACT TGA Thr GAT CTA Asp 440 CCT GGA	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT	TCT Arg GAT CTA Asp 00 TAT ATA Tyr 1450 GAG CTC	GAC CTG Asp GCA CGT Ala CCA GGT Pro	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC	GGT Pro GGC CCG Gly 410 ATG TAC Met 146 CTC GAG	TAT ATA Tyr CTG GAC Leu AAC TTG Asn TTG AAC	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP	GTG CAC Val TGG ACC Trp GCT CGA Ala 170 GAC CTG	TCC AGG Ser 1: CCC GGG Pro CCG GGC CCG Gly CCT GGA	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg	AGC TCG Ser GAG CTC Glu	TGT ACA Cys> TCT AGA Ser> CTG GAC	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1390 GCTC CCA	AGT TCA Ser ACT TGA Thr GAT CTA Asp 440 CCT GGA	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT	TCT Arg GAT CTA Asp 00 TAT ATA Tyr 1450 GAG CTC	GAC CTG Asp GCA CGT Ala CCA GGT Pro	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC	GGT Pro GGC CCG Gly 410 ATG TAC Met 146 CTC GAG	TAT ATA Tyr CTG GAC Leu AAC TTG Asn TTG AAC	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP	GTG CAC Val TGG ACC Trp GCT CGA Ala 170 GAC CTG	TCC AGG Ser 1: CCC GGG Pro CCG GGC CCG Gly CCT GGA	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg GCT CGA	AGC TCG Ser GAG CTC Glu	TGT ACA Cys> TCT AGA Ser>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1390 GCTC CCA	AGT TCA Ser ACT TGA Thr GAT CTA ASP 440 CCT GGA Pro	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT	GAT CTA Asp 00 TAT ATA Tyr 1450 GAG CTC Glu	GAC CTG Asp GCA CGT Ala CCA GGT Pro	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC	GGT Pro GGC CCG Gly 410 ATG TAC Met 146 CTC GAG Leu	TAT ATA Tyr CTG GAC Leu AAC TTG ASN TTG AAC Leu	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP	GTG CAC Val TGG ACC Trp GCT CGA Ala 470 GAC CTG Asp	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly CCT GGA Pro	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg GCT CGA	AGC TCG Ser GAG CTC Glu L480 TTT AAA Phe	TGT ACA Cys> TCT AGA Ser> CTG GAC Leu>	
ATG TYT 1340 GTG CAC Val 1390 GAG CTC Glu 10 GGT CCA Gly	AGT TCA Ser ACT TGA Thr GAT CTA ASP 440 CCT GGA Pro	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP	GTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT Ser	TCT Arg GAT CTA Asp 00 TAT ATA Tyr 1450 GAG CTC Glu	GAC CTG Asp GCA CGT Ala CCA GGT Pro GAT CTA Asp	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC Leu	GGT Pro GGC CCG Gly 410 ATG TAC Met 146 CTC GAG Leu	TAT ATA Tyr CTG GAC Leu AAC TTG ASn 50 TTG AAC Leu	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu GTC CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP 14 ACA TGT Thr	GTG CAC Val TGG ACC Trp GCT CGA Ala 170 GAC CTG Asp	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly CCT GGA Pro	TAA Ile 380 TGT ACA Cys 143 AGA TCT Arg GCT CGA Ala	AGC TCG Ser GAG CTC Glu L480 TTT AAA Phe	TGT Thr> TGT ACA Cys> TCT AGA Ser> CTG GAC Leu>	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1390 GGT CCA GTG CTA CCA CTC	AGT TCA Ser ACT TGA Thr GAT CTA ASP 440 CCT GGA Pro	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP AAT TTA ASN	CTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT Ser	GAT CTA Asp 00 TAT ATA Tyr 1450 GAG CTC Glu	GAC CTG Asp GCA CGT Ala CCA GGT Pro GAT CTA Asp	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC Leu	GGT Pro GGC CCG Gly 410 ATG TAC Met 14 CTC GAG Leu	TAT ATA TYr CTG GAC Leu AAC TTG ASn TTG AAC Leu 1510 GGT	GGT CCA Gly 13: TGT ACA Cys CTG GAC Leu GTC CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP 14 ACA TGT Thr	TGG ACC Trp GCT CGA Ala 470 GAC CTG ASP 152 CTT	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly CCT GGA Pro 20 GGG	TAA Ile 80 TGT ACA Cys 143 AGA TCT Arg GCT CGA Ala	AGC TCG Ser GAG CTC Glu 1480 TTT AAA Phe 15	TGT Thr> TGT ACA Cys> TCT AGA Ser> CTG GAC Leu> 530 CCA	
ATG Tyr 1340 GTG CAC Val 1390 GAG CTC Glu 1390 GGT CCA Gly TCT AGA	AGT TCA Ser ACT TGA Thr GAT CTA ASP 440 CCT GGA Pro 141 TGT ACA	GAG CTC Glu 13 GTG CAC Val GAT CTA ASP AAT TTA ASN	CTC Glu 350 GGA CCT Gly 140 GGC CCG Gly TCA AGT Ser TGT ACA	GAT CTA Asp 00 TAT ATA TYT GAG CTC Glu CTC CAG	GAC CTG Asp GCA CGT Ala CCA GGT Pro GAT CTA Asp	CGG GCC Arg 1360 GAG CTC Glu 14 GCC CGG Ala CTG GAC Leu	GGT Pro GGC CCG Gly 410 ATG TAC Met 146 CTC GAG Leu AGT	TAT ATA TYr CTG GAC Leu AAC TTG ASN TTG AAC Leu 1510 GGT CCA	GGT CCA Gly 13 TGT ACA Cys CTG GAC Leu GTC CAG Val	GAC Leu 70 GTC CAG Val 1420 GAT CTA ASP ACA TGT Thr AGG TCC	GTG CAC Val TGG ACC Trp GCT CGA Ala 170 GAC CTG Asp 152 CTT GAA	TCC AGG Ser 1: CCC GGG Pro GGC CCG Gly CCT GGA Pro 20 GGG CCC	TAA Ile 80 TGT ACA Cys 143 AGA TCT Arg GCT Arg GCT CGA Ala	AGC TCG Ser GAG CTC Glu L480 TTT AAA Phe TCC AGG	TGT Thr> TGT ACA Cys> TCT AGA Ser> CTG GAC Leu>	

Figure 3D

1540 1550 1560 1570 GGC AGC CTA CTG GAC AGG TTG AGG CTG TCA TTT GCA AAG GAA GGG GAC CCG TCG GAT GAC CTG TCC AAC TCC GAC AGT AAA CGT TTC CTT CCC CTG Gly Ser Leu Leu Asp Arg Leu Arg Leu Ser Phe Ala Lys Glu Gly Asp> 1580 1590 1600 1610 TGG ACA GCA GAC CCA ACC TGG AGA ACT GGG TCC CCA GGA GGG GGC TCT ACC TGT CGT CTG GGT TGG ACC TCT TGA CCC AGG GGT CCT CCC CCG AGA Trp Thr Ala Asp Pro Thr Trp Arg Thr Gly Ser Pro Gly Gly Gly Ser> 1630 1640 1650 1660 1670 GAG AGT GAA GCA GGT TCC CCC CCT GGT CTG GAC ATG GAC ACA TTT GAC CTC TCA CTT CGT CCA AGG GGG GGA CCA GAC CTG TAC CTG TGT AAA CTG Glu Ser Glu Ala Gly Ser Pro Pro Gly Leu Asp Met Asp Thr Phe Asp> 1680 1690 1700 1710 AGT GGC TTT GCA GGT TCA GAC TGT GGC AGC CCC GTG GAG ACT GAA TCA CCG AAA CGT CCA AGT CTG ACA CCG TCG GGG CAC CTC TGA CTA CTT Ser Gly Phe Ala Gly Ser Asp Cys Gly Ser Pro Val Glu Thr Asp Glu> 1730 1740 1750 1760 1770 GGA CCC CCT CGA AGC TAT CTC CGC CAG TGG GTG GTC AGG ACC CCT CCA CCT GGG GGA GCT TCG ATA GAG GCG GTC ACC CAC CAG TCC TGG GGA GGT Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Arg Thr Pro Pro> 1780 1790 CCT GTG GAC AGT GGA GCC CAG AGC AGC TAG GGA CAC CTG TCA CCT CGG GTC TCG TCG ATC Pro Val Asp Ser Gly Ala Gln Ser Ser ***>

Figure 4A Human Ig heavy chain locus (total length ≈1Mb, not drawn to scale):



loxP

PGK-neo

PGK-hyg

lox511 loxP